

Multi-electrode recordings in children with dystonia: widespread activation in basal ganglia and thalamus

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Abstract

Rationale: The optimal target for DBS in children with non-DYT1 dystonia is not known, and it is likely that the best target may vary depending on the etiology and distribution of injury in each child.
Method: We evaluate DBS targets using stimulation and recording from temporary depth electrodes with 160 contacts implanted in basal ganglia and thalamus
Results: Microelectrode recordings show widespread nonsynchronous spike activity.
Conclusion: Dystonic muscle contraction is associated with nonspecific and often bilateral activation throughout pallidum and thalamus.

Methods

10 Adtech depth electrodes record simultaneously from 160 channels in GPi, STN, and thalamus VA, Vo, Vim, or VPL in awake children 24 hours per day for up to 1 week. We perform test stimulations to predict the effect of permanent DBS implantation. 60 low-impedance channels record LFP, 100 high-impedance microelectrode channels record 2-5 spiking units per contact, as well as micro-LFP background signals.

Results

Recording: Baseline firing rates are low at rest.
Single-units: nonsynchronous widespread activity during contraction.
LFP: wideband activity during contraction.
Clinical: The optimal stimulation target varied between children.
All children received 4 leads, usually bilateral GPi + bilateral thalamus.
Thalamus: immediate effect on **hyperkinetic** movements.
GPi: delayed effect on **hypertonia**.

Conclusion

Physiology: Dystonia is characterized by widespread asynchronous activity (vs. synchronized rhythmic activity in epilepsy). DBS causes broadly synchronous rhythmic activity. Since DBS improves symptoms, this suggests that asynchronous activity is causative of dystonia.
Clinical: The new method of DBS targeting identified targets that varied between children. Beneficial effects exceed what would be expected for GPi stimulation alone. Therefore this method may increase the effectiveness of DBS in non-DYT1 dystonia and may allow it to be applied to a broader range of children including those with diagnoses not previously known to respond to stimulation.

Details

We present 7 results from a new technique for determining optimal neuro-anatomical targets. Up to 10 Adtech™ MM16C depth electrodes are implanted in each child in multiple brain regions, including subthalamic nucleus (STN), internal globus pallidus (GPi), and thalamus: ventro-anterior nucleus (VA), ventral oralis nucleus (Voa/Vop), ventral intermediate nucleus (Vim), and ventroposterolateral nucleus (VPL). Each electrode has up to 10 high-impedance “micro” contacts capable of identifying single unit firing, and 6 “macro” contacts capable of identifying local field potentials and through which test stimulation can be performed. Children are monitored for up to 1 week in the epilepsy monitoring unit with continuous and simultaneous recording from up to 160 contacts (AlphaOmega Inc. NeuroOmega™ or TDT recording system), and bipolar stimulation at macro contacts during attempts at movement.

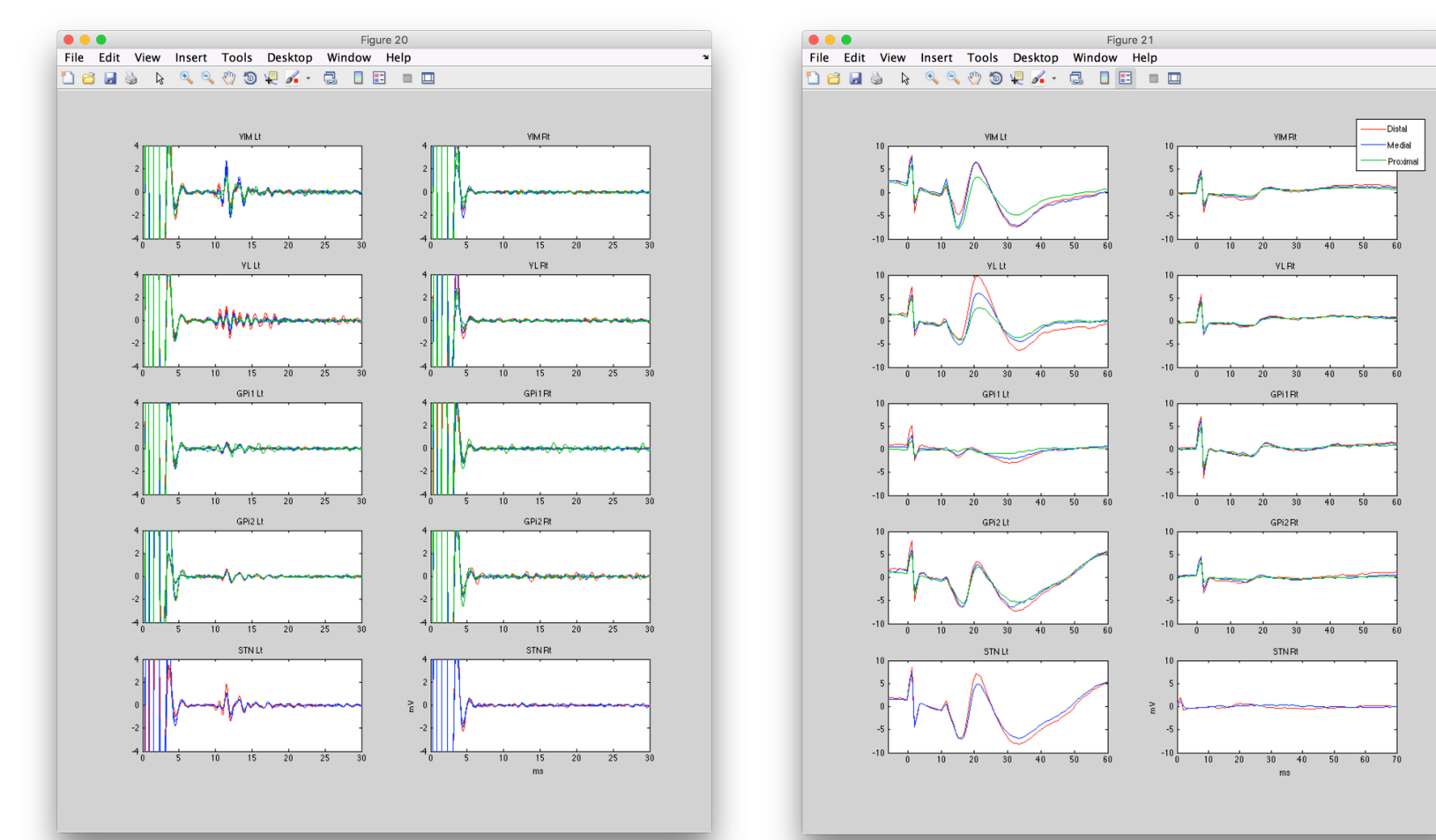
<u>7 years, striatal necrosis</u>	Implanted GPi+Vim bilateral. Resolution of severe painful spasms. Body relaxation. Improved voluntary hand movement.
<u>18 years, cerebral palsy</u>	Implanted GPi+STN bilateral. Better posture, reduced spasms, improved sleep.
<u>6 years, hemolytic-uremic yndrome.</u>	Implanted GPi+Vo thalamus bilateral. Improved posture and balance.
<u>14 years, hemidystonia</u>	Implanted unilateral Vo, VPL, GPi. Improved hand function. Eliminated hyperkinetic/ballistic shoulder and arm movements.
<u>19 years, kernicterus</u>	Pre-existing GPi leads. Implanted new bilateral Vo. Reduced hyperkinetic movements and better speech and facial movement.
<u>15 years, striatal atrophy</u>	Implanted GPi + Vim bilateral. Resolution of torticollis, improved bilateral hand function. Improved gait and speech.
<u>20 years, cerebral palsy</u>	Implanted GPi + Vo bilateral. Recently implanted.

Observations

1. Dystonic spasms -> activation throughout several nuclei, including GPi, Vo, and Vim.
2. Overflow is associated with both ipsilateral and contralateral thalamic activation.
3. Baseline firing rates are very low, but not zero.
4. Optimal target for clinical efficacy varies between children.

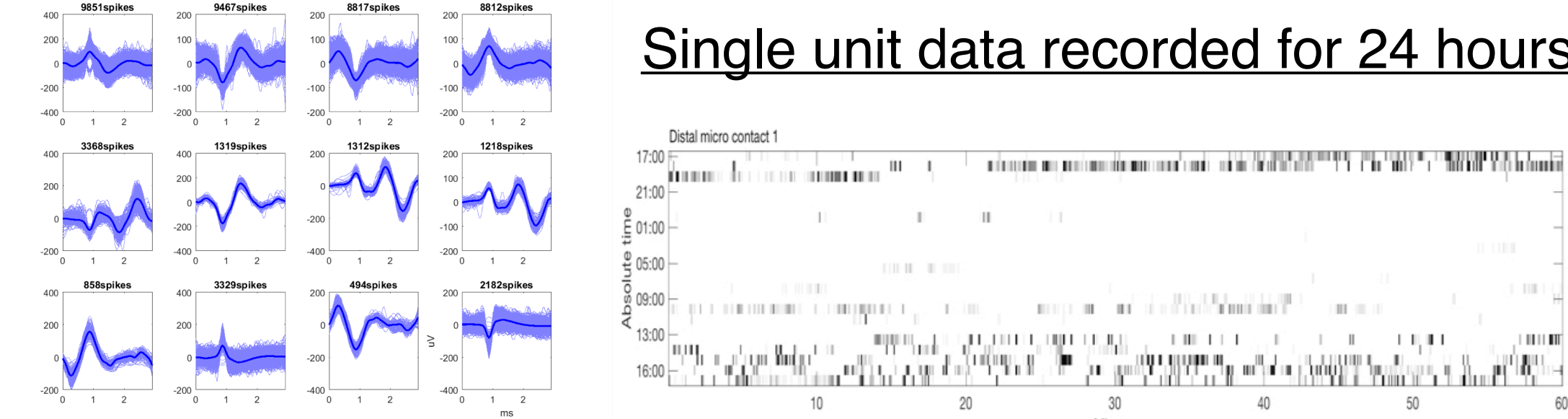
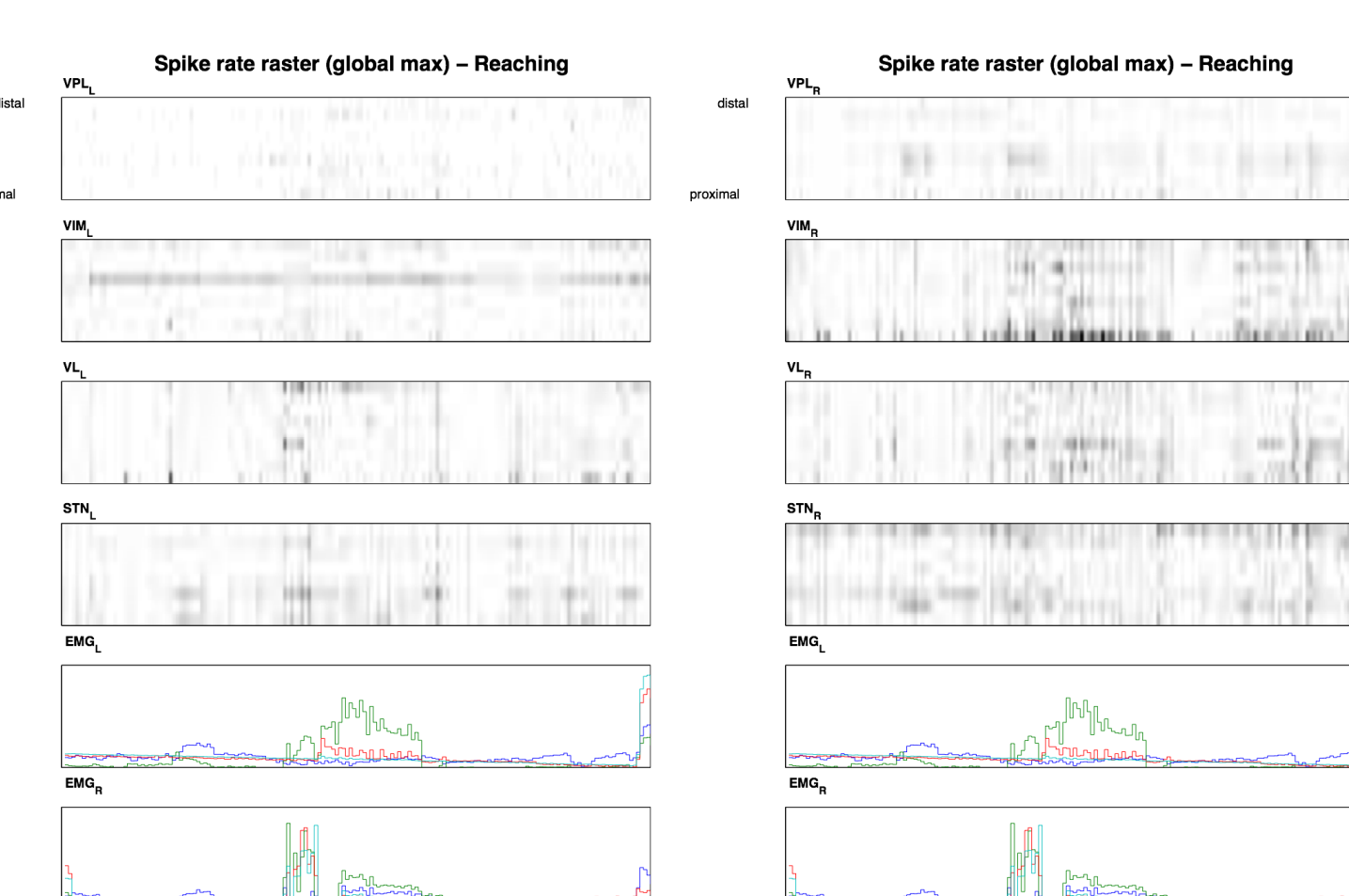
Somatosensory Evoked Potential

Stimulation of Median nerve at the wrist causes a robust response in Vim that can be used to confirm location of this nucleus.



19 years, Kernicterus

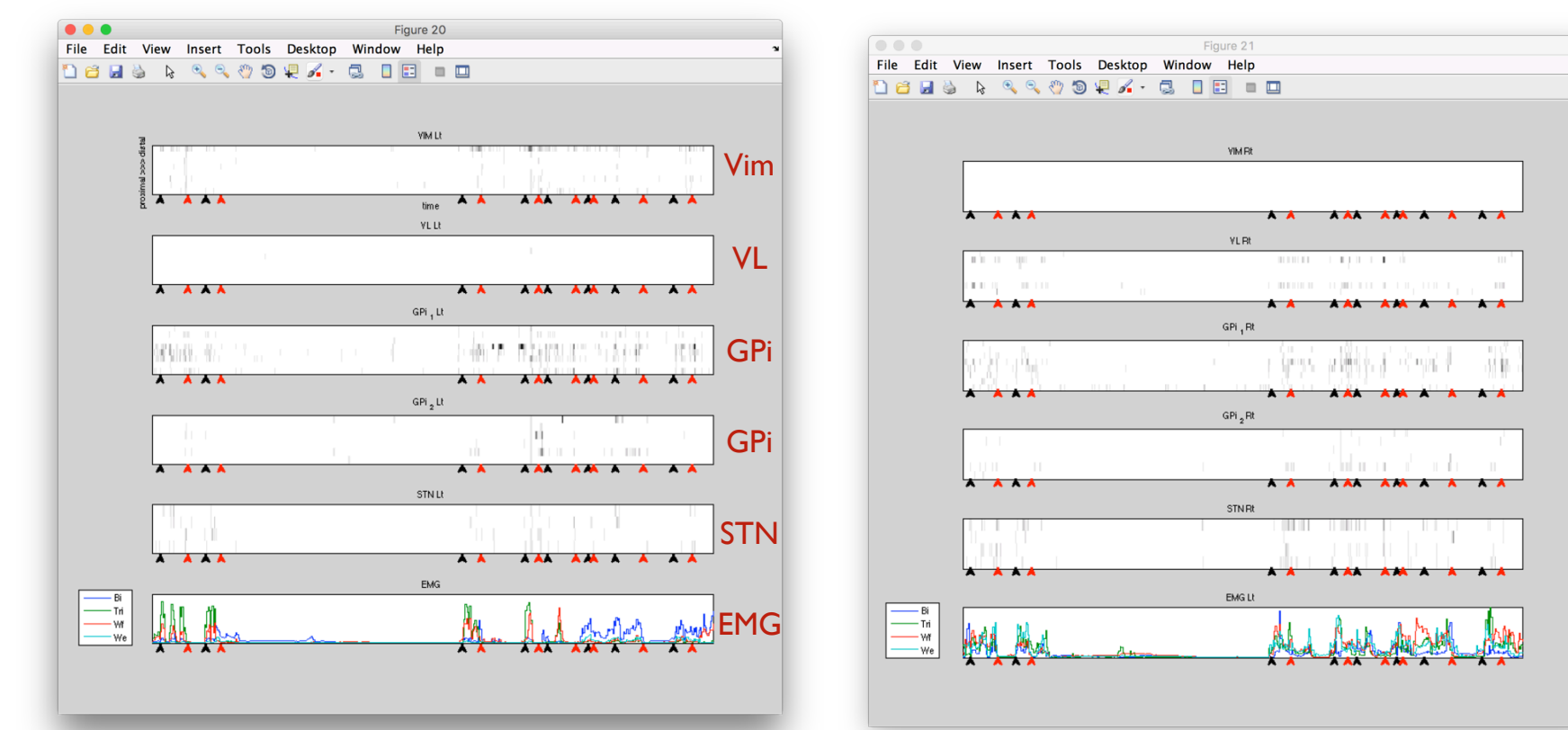
Broad spread of activation through multiple deep nuclei.



Single unit data recorded for 24 hours

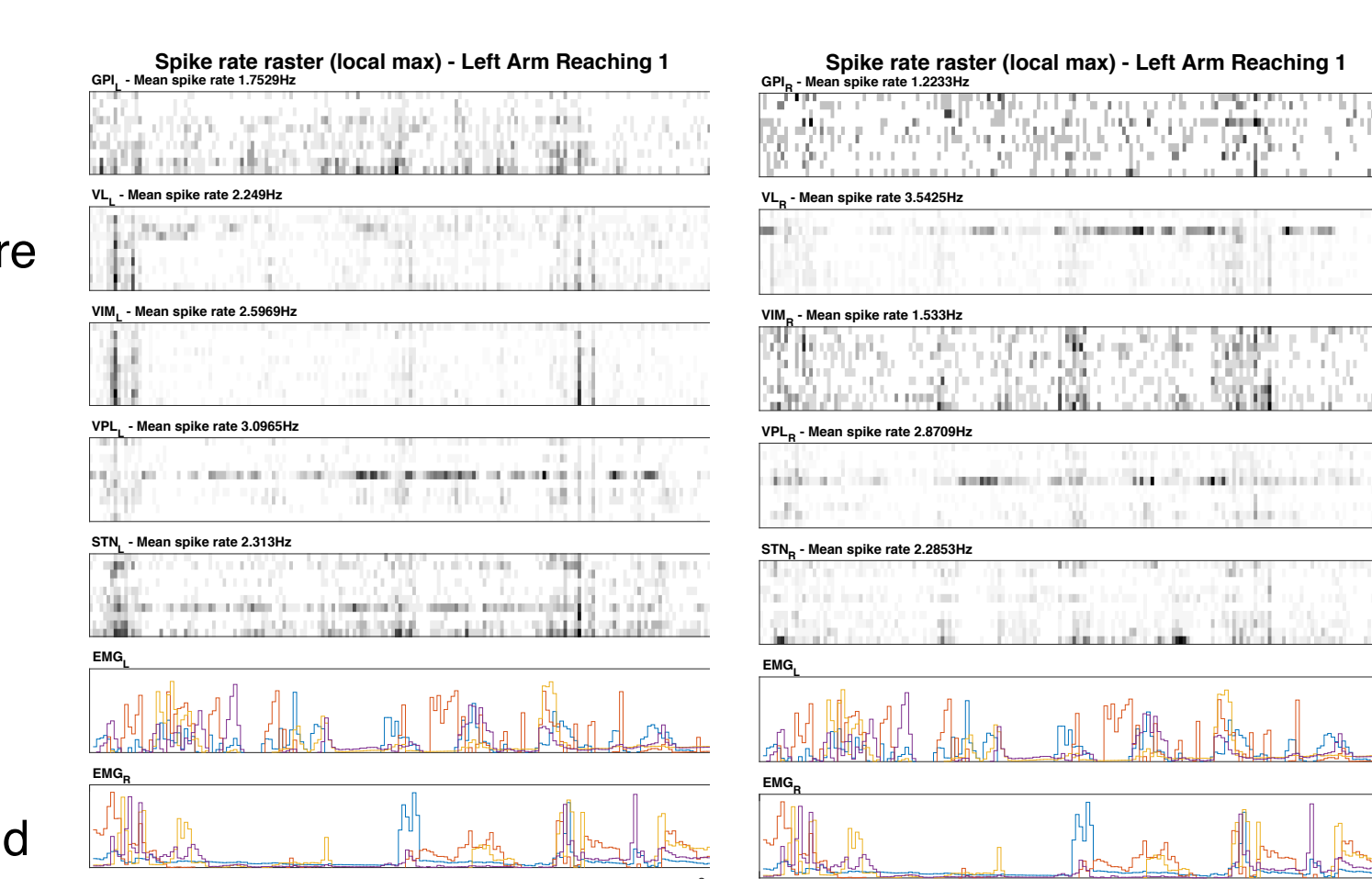
7 years, Striatal Necrosis

Bilateral activation during spontaneous dystonic spasms.



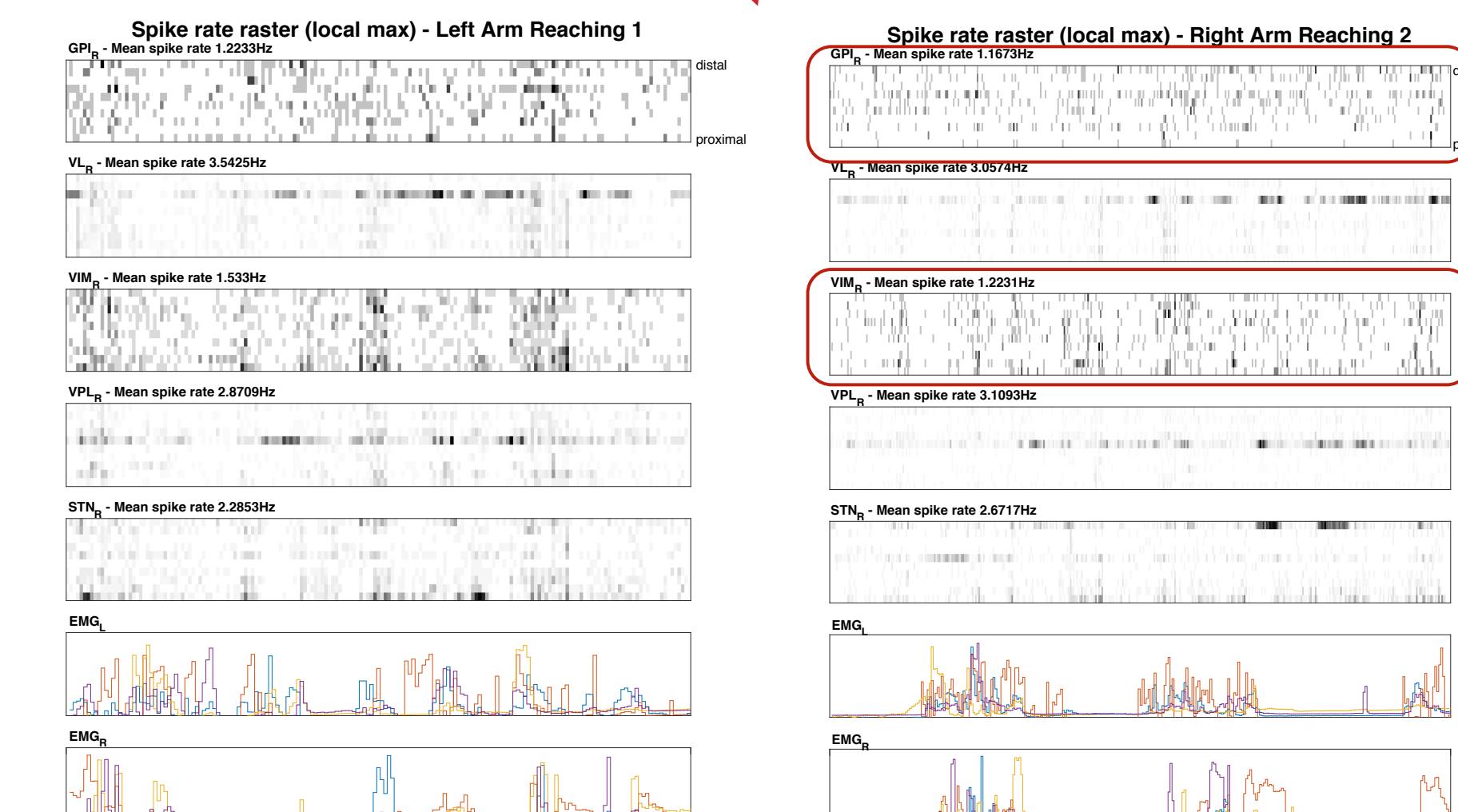
15 years, striatal atrophy

During Left arm reaching,...
..Left VL, Vim, STN are active when there is overflow on the right.
..Right Vim, STN are more active when there is overflow on the right.
=> overflow is associated with **bilateral** thalamus and basal ganglia activation



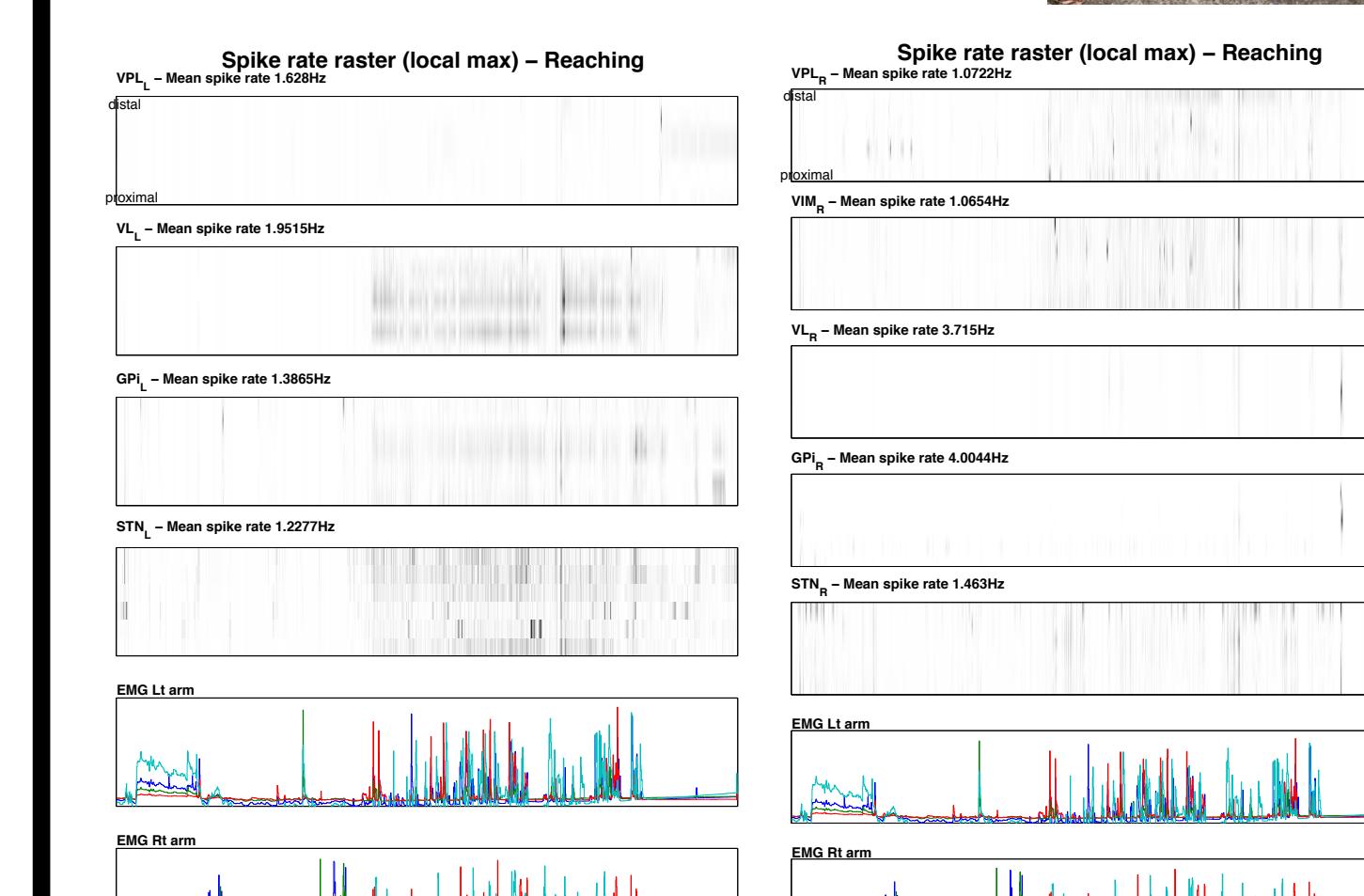
14 years, Hemidystonia

Broad activation through multiple deep nuclei during contralateral and **ipsilateral** movement.

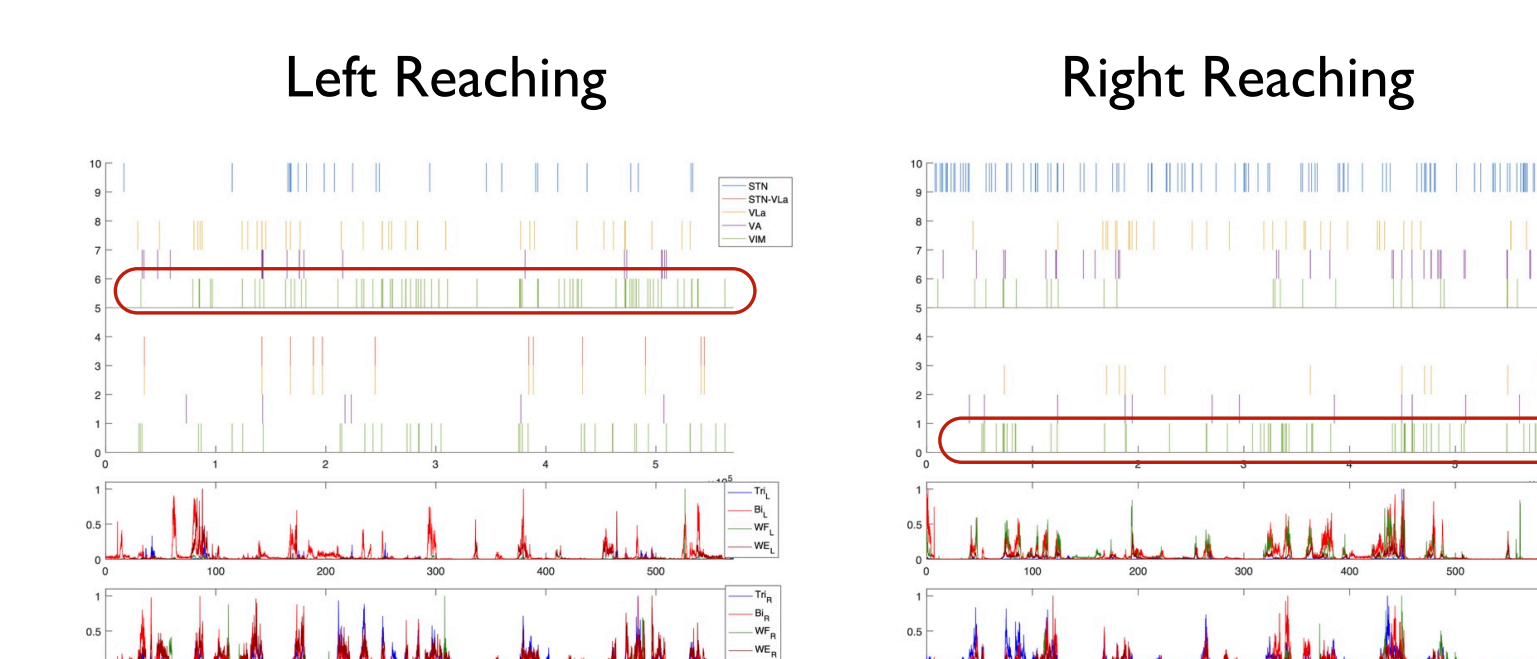


6 years, Hemolytic-Uremic Syndrome

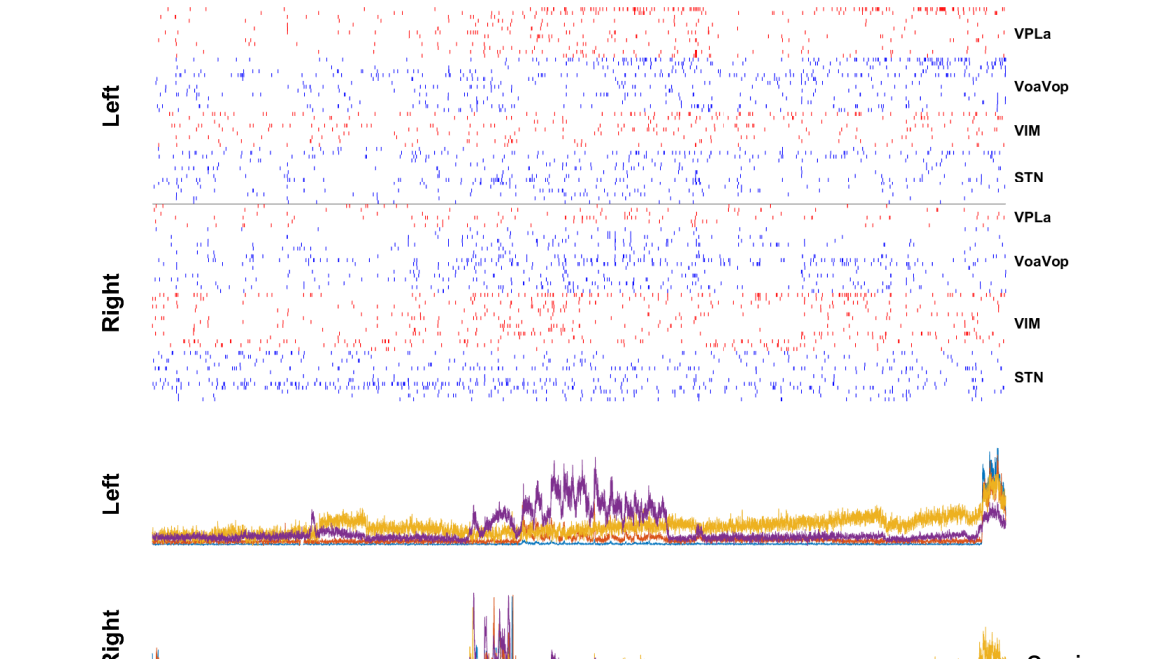
During right arm reaching...
..Left Vo, GPi, STN active
..Right VPL, Vim active
=> overflow to left arm associated with overflow in right Vim and VPL.



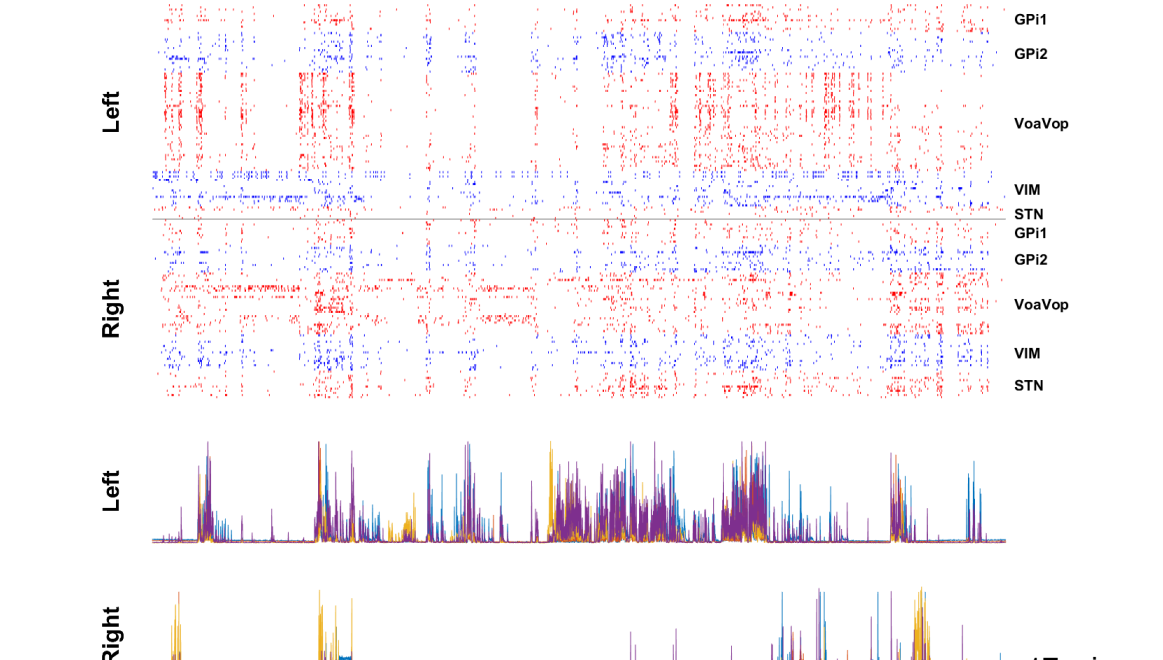
Overflow can be associated with ipsilateral Vim activity, suggesting a role for cerebellum in contralateral muscle activation.



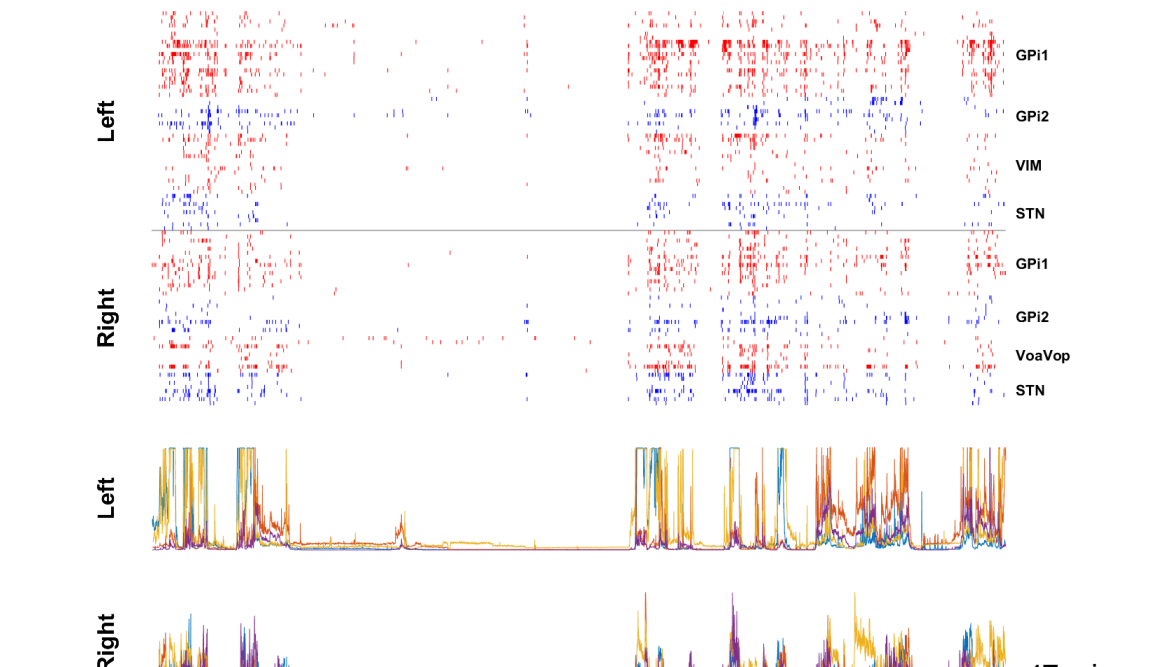
Kernicterus: Relatively high background activity increases in contralateral Vo/Vim and ipsilateral STN/VPL during left arm movement.



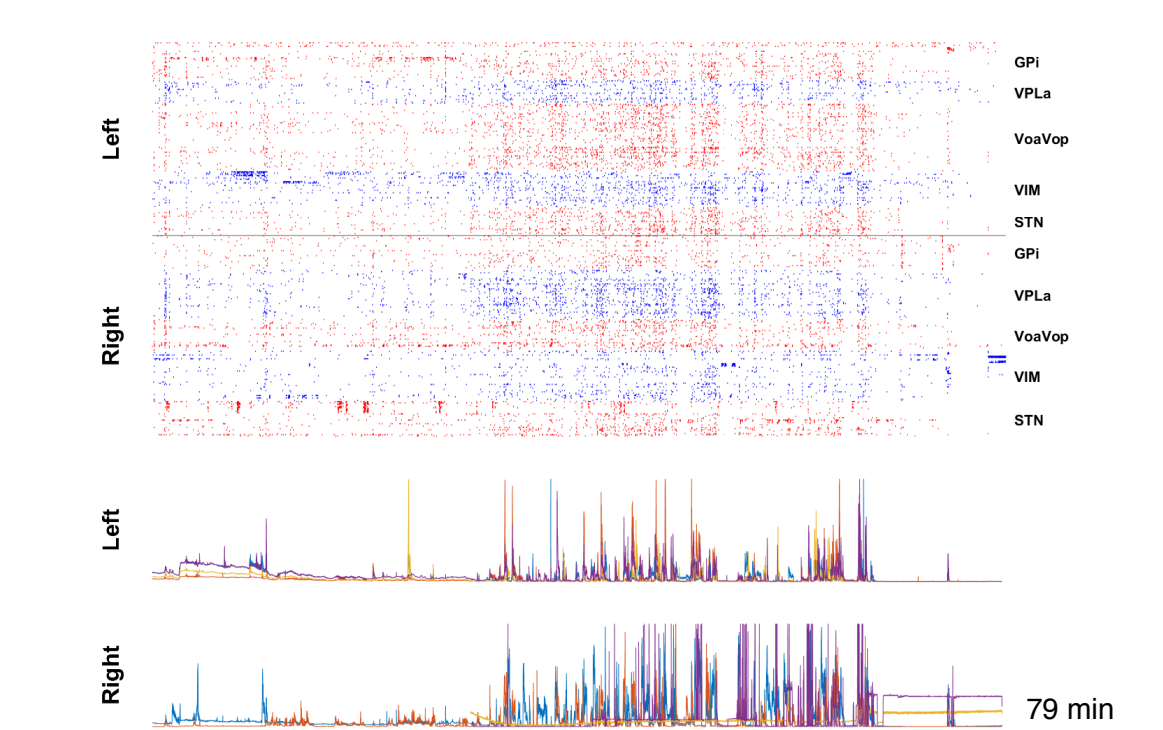
Dyskinetic CP: Bilateral activity closely correlated with unilateral EMG during left arm movement. Ipsilateral activation in Vo correlates with overflow to right-sided muscles.



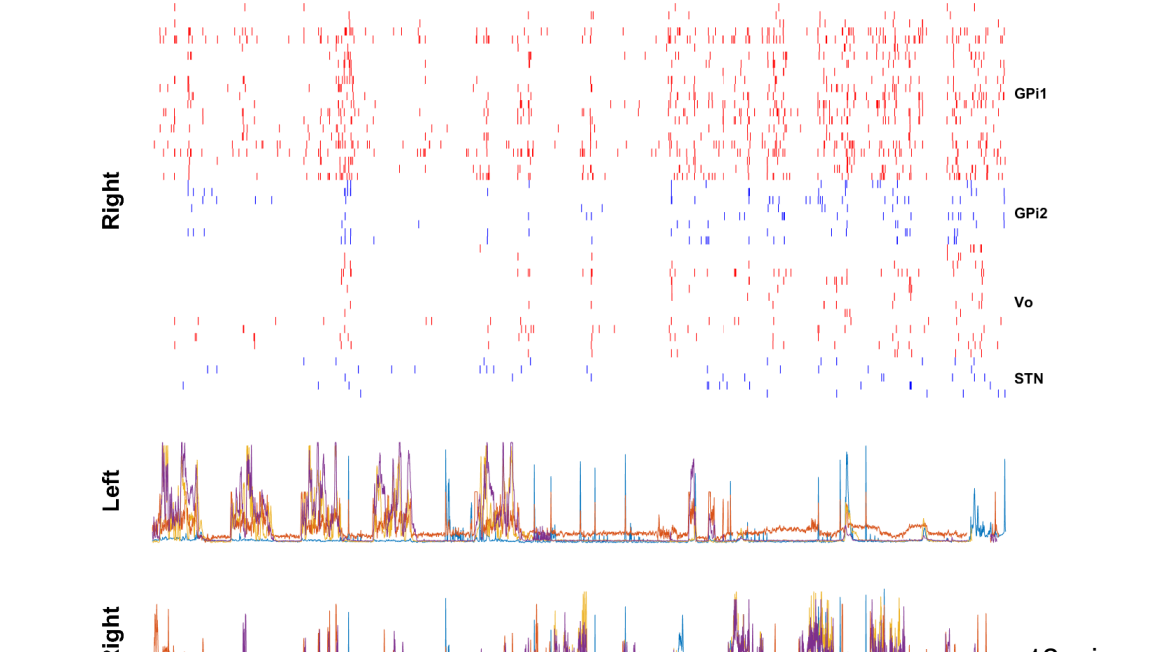
Striatal Necrosis: Bilateral activity closely correlated with unilateral EMG during attempted right arm movement. Ipsilateral activation in GPi, Vo, and STN could be responsible for left emg overflow.



Hemolytic-Uremic syndrome: Overflow during right arm movement associated with widespread ipsilateral activation.



Left hemidystonia: high activation in right GPi during both left hand grips (first half) and right hand grips (second half).



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Pediatric DBS consortium



pedidbs.org

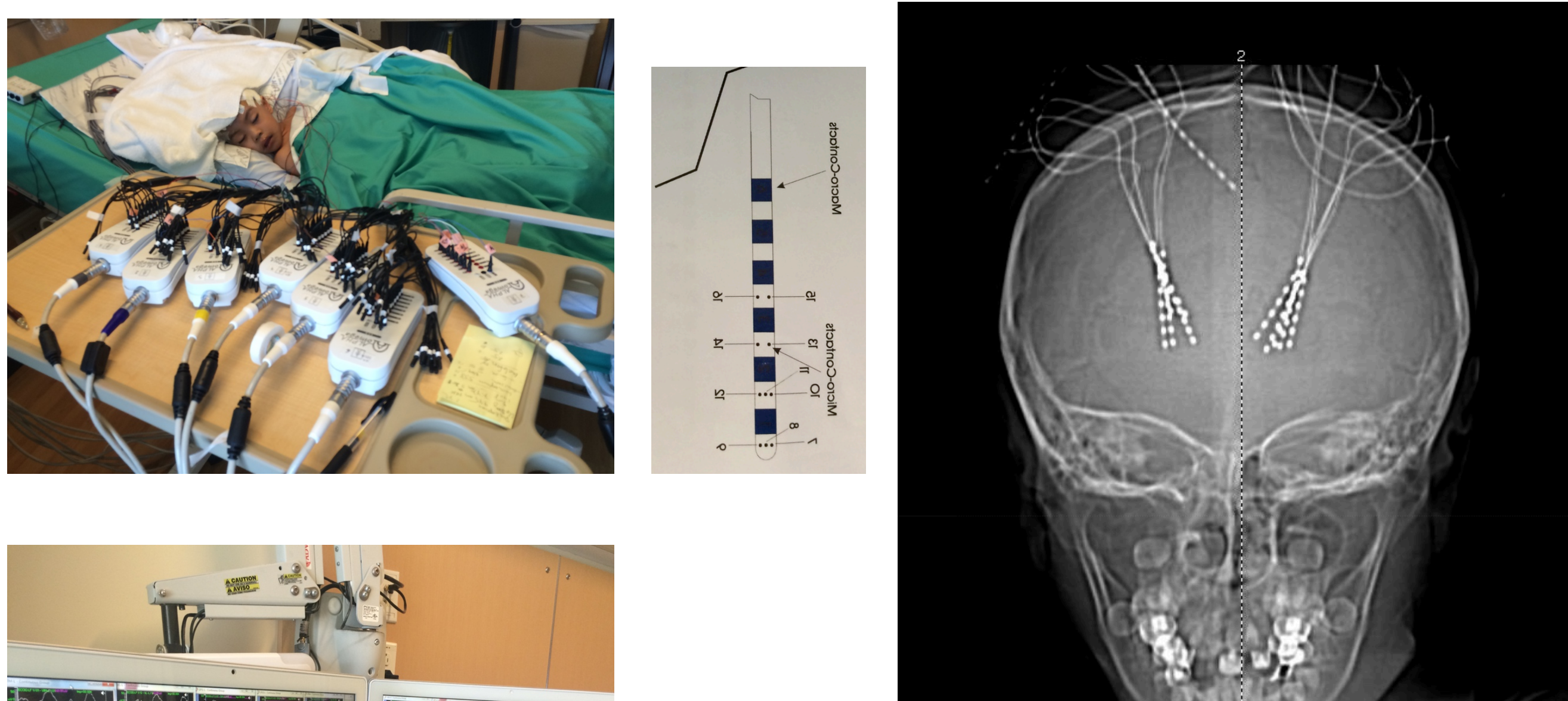
Pediatric Special Interest Group



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Stimulation through macro-contacts.
Recording single units + LFPs through micro-contacts.
5 days continuous bedside recording.